IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 09/640,582

Applicant: Baumann et al.

Filed: August 17, 2000

TC/AU: 1649

Examiner: Michael T. Brannock

Docket No.: 205970 (Client Reference No. PA29237 US-03138/cel)

Customer No.: 23460

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Dear Sir:

Applicants request review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a Notice of Appeal.

The review is requested for the reasons stated on the following sheets.

Respectfully submitted,

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Date: April 19, 2006

MAILING/TRANSMISSION CERTIFICATE UNDER 37 CFR 1.8 OR 1.10			
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Name (Print/Type)	John Kilyk, Jr.		
Signature		*Date*	April 19, 2006

REASONS FOR PRE-APPEAL BRIEF REQUEST FOR REVIEW

Status of Claims

Claims 3 and 16-18 are currently pending, stand rejected, and are the subject of the appeal. Claims 1, 2, 4-15, and 19-46 were previously cancelled.

Summary of Claimed Subject Matter

The claims are directed to an isolated or purified human nucleic acid comprising the nucleotide sequence of SEQ ID NO: 1 (see, e.g., the specification at page 29).

Grounds of Rejection to be Reviewed

Claims 3 and 16-18 are rejected under 35 U.S.C. §§ 101 and 112, first paragraph, because the claimed invention allegedly is not supported by either a specific and substantial asserted utility or a well-established utility.

Reasons for Withdrawal of Rejection

The appealed claims are directed to a human nucleic acid sequence which encodes an I_h ion channel, which is also known as the hyperpolarization-activated, cyclic nucleotide-gated channel subunit 2 (HCN2) gene. In essence, the Examiner alleges that the claimed invention lacks a specific and substantial utility or a well-established utility because one of ordinary skill in the art would not have known what disorder(s) could be treated using the claimed nucleic acid sequence at the time of the filing of the subject application.

Evidence of pharmacological or other biological activity of a compound is relevant to an asserted therapeutic use if there is a *reasonable correlation*, not necessarily a statistical certainty, between the activity in question and the asserted utility. *Cross v. Iizuka*, 753 F.2d. 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985); *In re Jolles*, 628 F.2d. 1322, 206 U.S.P.Q 885 (C.C.P.A. 1980); *Nelson v. Bowler*, 626 F.2d. 853, 206 U.S.P.Q. 881 (C.C.P.A. 1980).

Appellants have previously demonstrated that the claimed invention has an asserted utility that is specific, substantial, and credible as prescribed in M.P.E.P. § 2107.01. In this regard, the asserted utility is specific in that the claimed nucleic acid sequence is disclosed as

being useful, for example, to treat and/or prevent cardiovascular disorders. Treatment and prevention of cardiovascular disease undoubtedly is a "real world" utility. Thus, the asserted utility also is substantial.

The specification of the subject application discloses a reasonable correlation between the activity of the I_h ion channel encoded by the claimed nucleic acid sequence and the asserted utility (see Reply to Office Action dated July 11, 2005). Moreover, Appellants provided documentary evidence supporting this reasonable correlation. For example, Ludwig et al., *EMBO J.*, 18, 2323-2329 (1999)), which published before the U.S. filing date of the subject application, confirms that SEQ ID NO: 1 encodes an I_h ion channel with cardiac pacemaker function (see, e.g., Ludwig reference at page 2327, first column).

Appellants further submit that the asserted utility is credible. The Examiner has provided no objective evidence that would cause one of ordinary skill in the art to doubt the asserted utility of the claimed invention. Instead, the Examiner alleges that neither the specification nor the art of record discloses any relationship between the claimed nucleic acid sequence and a disease or disorder that is treatable using the claimed nucleic acid sequence (see, e.g., Office Action dated January 24, 2005 at page 5, lines 11-14). The Examiner further alleges that the asserted utility is not specific for cardiovascular disease because one of ordinary skill in the art would have to conduct further experimentation to establish a nexus between the claimed nucleic acid sequence and any disease (see Office Action dated January 24, 2005, at page 5, lines 16-20). However, as indicated above, the specification of the subject application, as well as the secondary evidence provided by Appellants (e.g., the Ludwig reference), establishes a nexus between the claimed nucleic acid sequence and cardiovascular disease. As such, there would be no reason for one of ordinary skill in the art to question the asserted utility of the subject matter of the appealed claims.

The credibility of the asserted utility is confirmed by several references published after the filing of the subject application which demonstrate a direct role for the polypeptide encoded by the claimed nucleic acid sequence in cardiovascular disease. In this respect, Qu et al., *Circulation, 107*: 1106-1109 (2003), and Plotnikov et al., *Circulation, 109*: 506-512 (2004), disclose that overexpression of HCN2 (i.e., the protein encoded by the claimed nucleic acid sequence) functions as a biological pacemaker when delivered via an adenoviral

vector to the left atrium of a canine heart. Zicha et al., *Cardiovascular Research, 66*: 472-481(2005), also discloses the use of HCN proteins as biological pacemakers to treat dysrhythmias associated with congestive heart failure (CHF), and suggests the development of therapies that target HCN expression and/or HCN-based currents for the treatment of CHF-related dysrhythmias. In addition, Ludwig et al., *EMBO J., 22*: 216-224 (2003), demonstrates that mice deficient in the HCN2 gene suffer from sinus dysrhythmia, and concludes that defects in HCN2 likely lead to absence epilepsy and sinoatrial node dysfunction in humans.

In view of the forgoing, the claimed invention involves an asserted utility that is specific, substantial, and credible. Thus, Appellants request withdrawal of the rejection under Section 101. Because the appealed claims are supported by a specific, substantial, and credible utility, one of ordinary skill in the art would know how to make and use the invention defined by the appealed claims. Accordingly, the enablement rejection under Section 112, first paragraph, also should be withdrawn.